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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,492	08/18/2000	Gary Van Nest	377882000800	7136

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/642,492	VAN NEST ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,13-23,25-33 and 37-52* is/are pending in the application.

4a) Of the above claim(s) *43-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13-23,25-33 and 37-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

The request filed on December 22, 2004 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/642,492 is acceptable and a RCE has been established. An action on the RCE follows.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 13-23, 25-30, 32, 33 and 37-42 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using an ISS molecule comprising SEQ ID NO: 1, does not reasonably provide enablement for IS sequences that are shorter or do not conform to the enabled motif. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicant submits that the teachings of Fearon et al. do not apply to the instant claims since the compositions of Fearon et al. are different from those claimed. Applicant states that the teachings of Fearon et al. are drawn to optimization of immunomodulatory sequences as opposed to identifying sequences with some activity. Applicant states that optimizing the activity of a polynucleotide does not indicate a lack of enablement.

Applicant's arguments have been fully considered, but are found unpersuasive. The instant claims are drawn to a method that requires two components: (i) a complex comprising an

immunomodulatory polynucleotide (ISS) that has been complexed with an antigen. Fearon et al. teach an ISS complexed to another molecule, cPLGA. The instant claims additionally require a second component, (ii) a second antigen. Fearon et al. additionally teach the activity of ISS molecules that are uncomplexed. Therefore, free ISS and complexed ISS molecules of Fearon et al. are comparable to the instant ISS-complexes and antigens that are uncomplexed with ISS.

Contrary to applicant's assertions, the teachings of Fearon et al. are drawn to identifying polynucleotides with ISS activity, see the sequences in Figure 2 and the paragraph bridging pages 2115-2116 for example. Although Fearon et al. also optimize the activity of short ISS by formulation with cPLGA, Fearon et al. also exemplify the unpredictability of immunostimulatory sequences. Previously, applicant pointed out the different activities of complexed versus uncomplexed ISS molecules from the teachings of Fearon et al. Since the instant claims require uncomplexed and complexed antigens administered with ISS molecules, the unpredictable nature of these molecules, exemplified by Fearon et al., is pertinent to the instant claims. Further, Fearon et al. clearly show that just because an ISS molecule has two CpG motifs present (see the first paragraph of section 2.2), the determination of whether it possesses immunomodulatory effects cannot be determined without experimentation. In fact, the sequence ACGTTCG of Fearon et al. comprises two CpG motifs and is only one amino acid short of the second amino sequence listed in claim 30 (which is required to be immunogenic). However, this sequence is demonstrated to be non-immunogenic when in a complexed and non-complexed form, see Figure 2 of Fearon et al. The skilled artisan would be unable to predict which characteristics are required for a sequence to be immunostimulatory since ACGTTCG of Fearon et al. has two CpG motifs and is not immunogenic. Therefore, whether the genus of ISS molecules encompassed by

claims 1, 25-30 and 37 is immunogenic is unpredictable and would require an undue quantity of experimentation to determine which species within the broad genus is immunogenic, since the presence of a CpG motif does not automatically equate to immunogenicity.

Applicant also argues that some degree of unpredictability is permitted, depending on the level of guidance provided in the specification and knowledge in the art.

Applicant's statement is true. However, in the instant case, the specification only exemplifies the immunomodulatory capabilities of SEQ ID NO: 1. There is no teaching or guidance provided for shorter ISS sequences or whether they are immunostimulatory. The instant claims require that they be immunostimulatory and Fearon et al. teaches that at least one of the sequences claimed to be immunostimulatory, ACGTTCG, is not. Therefore, overcoming the level of unpredictability in the instant case would require an undue quantity of experimentation for the skilled artisan.

Applicant asserts that immunostimulatory molecules are well known in the art and cites patents that use ISS in methods of treatment.

Applicant's arguments have been fully considered, but are found unpersuasive. The instant ISS molecules claimed are required to be immunostimulatory, but there is no teaching provided in the specification that supports this assertion. Further, there is evidence from the teachings of Fearon et al. that immunostimulatory activity of ISS molecules is unpredictable and that a sequence containing two CpG motifs is not immunostimulatory. The patents discussed are not relevant to the instant case since the method of treatment is unrelated and the claimed compositions do not resemble the one instantly claimed.

Applicant points to teachings in the specification regarding how one of skill would be able to determine whether an ISS molecule is immunostimulatory.

However, the claims encompass a broad scope of ISS molecules that are required to be immunostimulatory. In addition, there is no teaching regarding an identifiable characteristic that would distinguish a non-immunostimulatory molecule from one that is immunostimulatory. The one example shown to be immunostimulatory, SEQ ID NO: 1, is not exemplary of the structural diversity or scope of ISS molecules claimed. For these reasons, it is maintained that the scope of immunostimulatory sequences claimed would require an undue quantity of experimentation for one skilled in the art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 13, 14, 17, 20-23, 25-33, 37 and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. (WO 98/55495, "Schwartz") **or** Carson et al. (WO 98/16247, "Carson"), as further evidenced by Horner et al. (Cellular Immunology. November, 1998; 190: 77-82) or Chu et al. (Journal of Experimental Medicine. 1997; 186 (10): 1623-1631) for reasons of record.

Applicant asserts that Schwartz et al. do not suggest the claimed method of co-administering an ISS-antigen conjugate and an unconjugated second antigen.

Applicant's arguments and a review of the reference have been considered, but are found unpersuasive. The instant claims are drawn to a method with two components: (i) an ISS-antigen complex and (ii) and un-complexed second antigen. On page 12, lines 29-31, Schwartz states that "[t]he ISS and the antigen...can be administered together in the form of a conjugate" (this teaching embraces (i) of the instant claims) "or co-administered in an admixture sufficiently close in time so as to modulate an immune response" (since the instant un-complexed second antigen is co-administered with the ISS complex, this phrase embraces (ii) of the instant claims). Schwartz also discusses these same concepts again on page 14, lines 8-14. Therefore, Schwartz et al. do suggest the instant composition claimed.

Applicant also argues that neither Schwartz or Carson provide motivation to the skilled artisan to administer a first antigen conjugate in an amount sufficient to modulate an immune response to a co-administered unconjugated second antigen. Applicant argues that Schwartz et al. and Carson et al. teach conjugated ISS-antigen molecules are more effective than unconjugated ones and that the skilled artisan would not be motivated to co-administer an unconjugated antigen.

Applicant's arguments have been fully considered, but are found unpersuasive. The claims are drawn to modulating an immune response to a second antigen by co-administering an ISS-antigen complex and a second antigen. The prior art cited clearly teaches that ISS-antigen complexes induce an immune response and that ISS/antigen mixtures induce an immune response. The immune response induced by an ISS/antigen mixture is an immuno-modulation against the unconjugated antigen, which is all that us required by the claims. Therefore, it is established by the prior art that the ordinary artisan would have a reasonable expectation of

modulating an immune response to an unconjugated, second antigen absent evidence to the contrary.

Claims 15 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. or Carson et al., as further evidenced by Horner et al. or Chu et al., as applied to claims 1, 11, 13, 14, 17, 20-23, 25-33, 37 and 40-42 above, and further in view of Lee et al. (Ann Med. 1998; 30: 460-468) for reasons of record.

Claims 16 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. or Carson et al., as further evidenced by Horner et al. or Chu et al., as applied to claims 1, 11, 13, 14, 17, 20-23, 25-33, 37 and 40-42 above, and further in view of Durali et al. (J of Virol. 1998; 72(5): 3547-3553) for reasons of record.

Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. or Carson et al., as further evidenced by Horner et al. or Chu et al., as applied to claims 1, 11, 13, 14, 17, 20-23, 25-33, 37 and 40-42 above, and further in view of Anderson (US Patent 4,673,574) for reasons of record.

Applicant argues that none of the references alone or in combination teach the instant invention or remedy the deficiencies of Schwartz et al. or Carson et al.

Applicant's arguments have been fully considered, but are found unpersuasive because there is no deficiency in the teachings of Schwartz et al. or Carson et al. The secondary references teach the limitations not taught by Schwartz et al. or Carson et al. and provide motivation to combine the elements with the composition of Schwartz et al. or Carson et al. with a reasonable expectation of success, absent evidence to the contrary.

Conclusion

This is a continuation of applicant's earlier Application No. 09/642,492. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 6:00 AM - 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Primary Examiner
Art Unit 1648